Title
Angiolymphoid hyperplasia with eosinophilia of the infra-axillary region: report of a case

Journal
Dermatology Online Journal, 20(3)

Authors
Parmar, Nisha V
Sandu, Jasleen
Kanwar, Amrinder J
et al.

Publication Date
2014

DOI
10.5070/D3203021755

Volume 20 Number 3
March 2014

Case Presentation

Angiolymphoid hyperplasia with eosinophilia of the infra-axillary region: report of a case

Nisha V. Parmar MD[1], Jasleen Sandhu MD[1], Amrinder J Kanwar MD FRCP[1], Uma Nahar Saikia MD[2]

Dermatology Online Journal 20 (3): 8

Departments of Dermatology, Venereology, and Leprology[1] and Histopathology[2] Post Graduate Institute of Medical Education and Research, Chandigarh-160012, India

Correspondence:

Nisha V. Parmar, MD
Department of Dermatology, Venereology, and Leprology
Post Graduate Institute of Medical Education and Research,
Chandigarh 160012, India
E-mail: parmarnish@gmail.com
Phone No: 91-9789277590

Abstract

Angiolymphoid hyperplasia with eosinophilia is an uncommon, benign hyperproliferative disorder. Papules and nodules occur predominantly in the head and neck region. Involvement of other sites such as the trunk and mucosae has been rarely reported. We herein report a case of angiolymphoid hyperplasia with eosinophilia involving the right infra-axillary region.

Introduction

Angiolymphoid hyperplasia with eosinophilia (ALHE) is a rare, benign angioproliferative disorder first described in 1969[1]. Its etiology is unknown and various hypotheses have been postulated. These range from ALHE being a reactive phenomenon to a benign neoplasm of endothelial cells. Angiolymphoid hyperplasia with eosinophilia has a female predilection and presents with reddish-brown firm papules and nodules commonly in the head and neck region. Occurrence at other sites is rare.

Case synopsis

A 45-year-old perimenopausal woman presented with a 2-year history of multiple reddish-brown papules and nodules in the right infra-axillary area. The lesions started as a single itchy reddish-brown papule 4-5 mm in size below the right axilla. Within 6 months, multiple similar lesions appeared around the initial papule and progressively increased in size to about 2-3 cms. They were pruritic and oozed blood on scratching. There was no preceding history of trauma or drug intake and the patient had no personal or family history of malignancy.

Physical examination revealed multiple reddish-brown papules and nodules, 0.5-2cm, clustered over an area of 12 x 8 cm in the right infra-axillary region (Figure 1). On palpation the lesions were firm and non-tender; they bled in a non-pulsatile fashion. There was significant right axillary lymphadenopathy in the form of two discrete firm non-tender freely-mobile lymph nodes of 2-3cm in the right central axillary group. Careful palpation of both the breasts revealed no lumps. Blood investigations revealed hemoglobin of 8gm%. Her absolute eosinophil count and serum immunoglobulin (Ig) E levels were within normal limits. Serology was negative for HIV. Mammography of both breasts revealed no lumps or calcification. Fine needle aspiration cytology of the right axillary nodes revealed reactive lymphoid hyperplasia. A skin biopsy was performed from one of the papules.

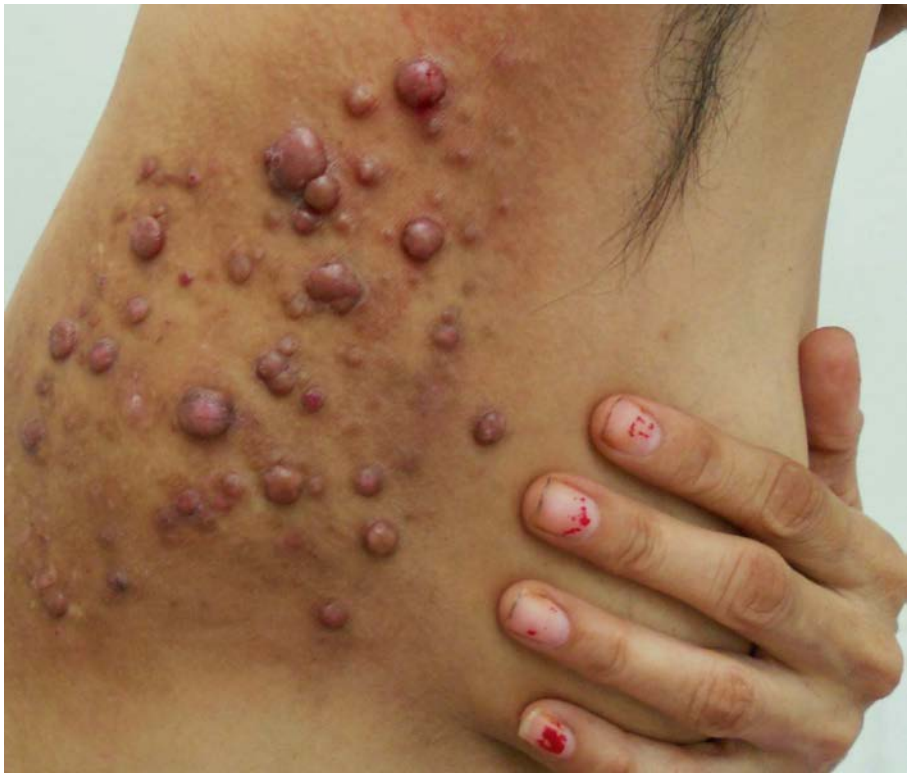

Figure 1. Multiple brown-red papules and nodules varying from 0.5cm to 2 cm grouped over an area of 12 by 8 cm in the right infra-axillary region

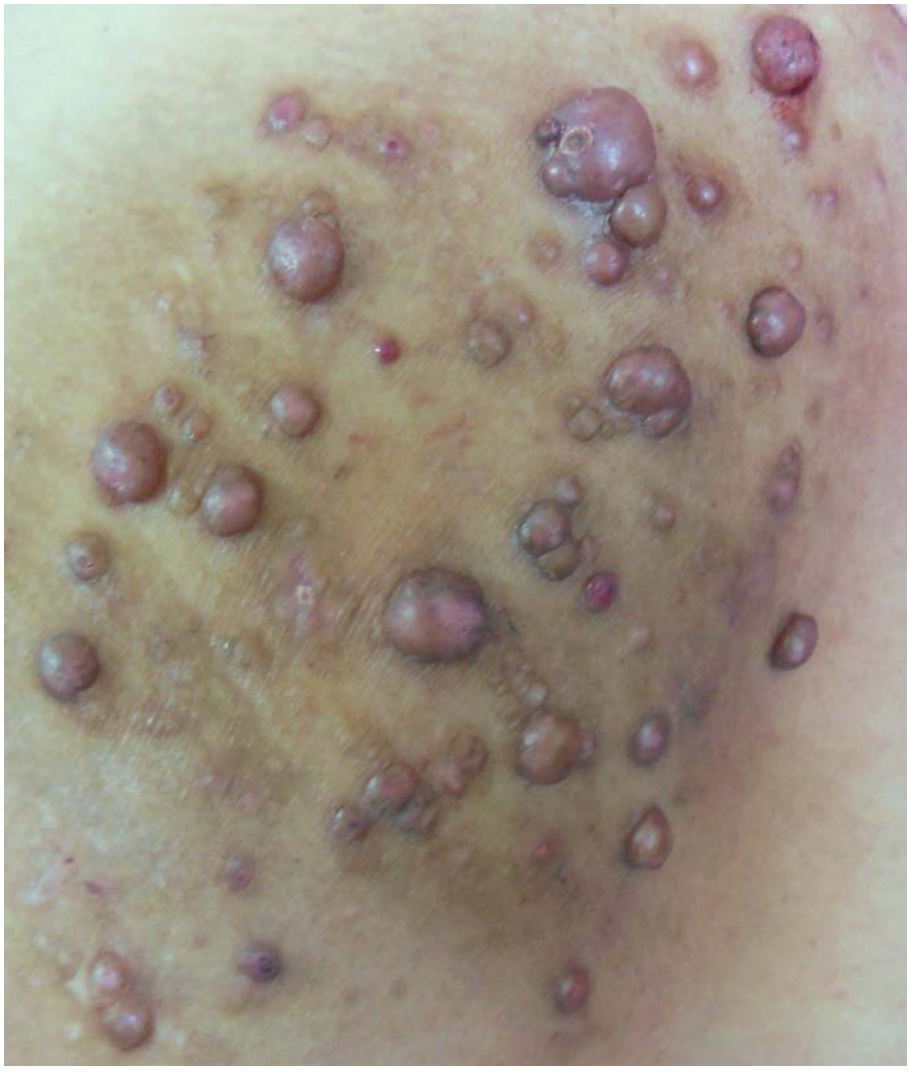

Figure 2. Close-up view of the papules and nodules; note the oozing of blood secondary to scratching on the uppermost nodule

Microscopic findings and clinical course

Hematoxylin and eosin-stained sections of the skin biopsy specimen showed well-circumscribed lobules consisting of small blood vessels with epithelioid endothelial cells protruding into the vascular lumen and a dense perivalscular infiltrate rich in lymphocytes and eosinophils.

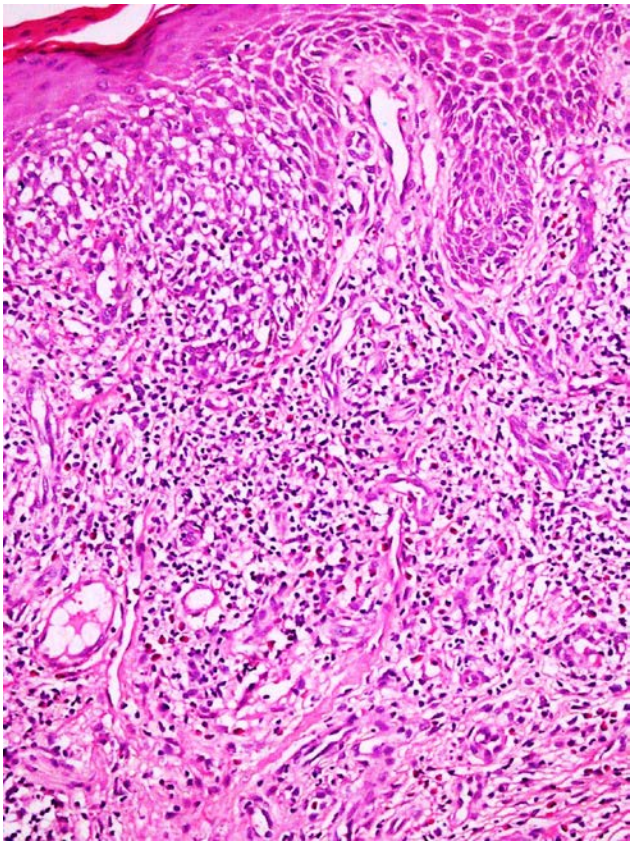

Figure 3. Lobular collection of lymphocytes and eosinophils in the upper dermis surrounding proliferating capillary channels abutting the epidermis (**H &Ex100**)

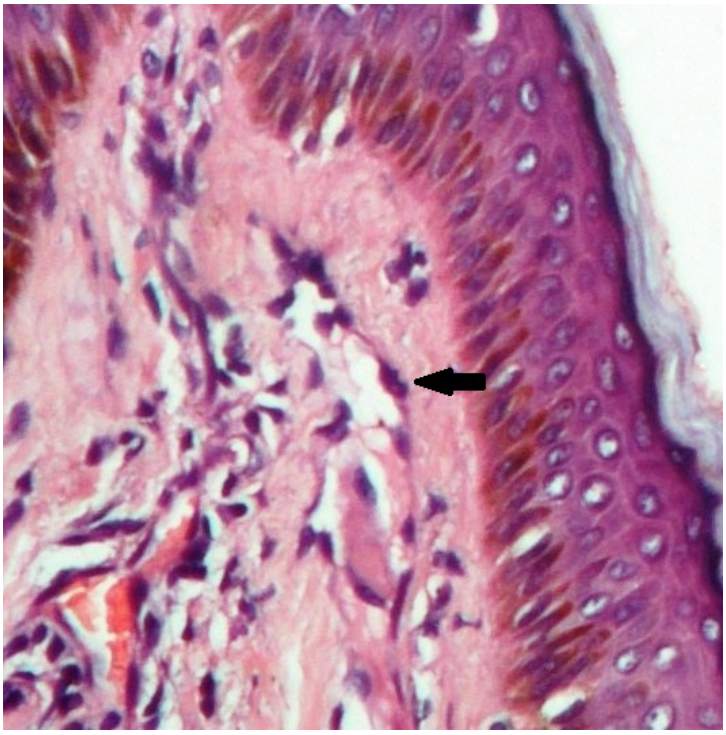

Figure 4. Capillaries with plump epithelioid endothelial cells (arrow) (**H &Ex400**)

The patient was treated with cryotherapy using liquid nitrogen spray. The freeze thaw cycles were repeated every 2 weeks. At the end of 10 weeks, there was improvement showing complete clearance of all lesions with residual post-inflammatory hypopigmentation (Figure 5).

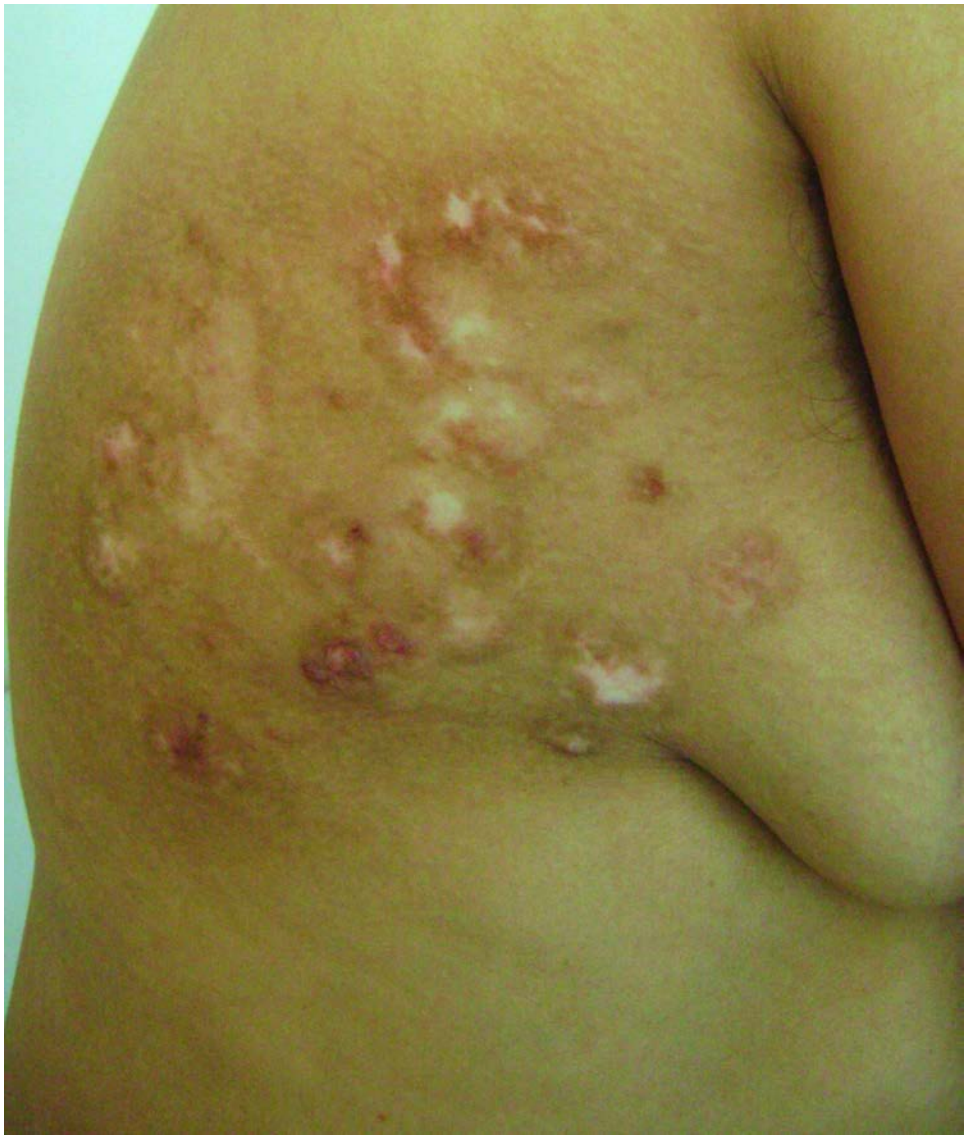

Figure 5. Post-treatment photo at the end of ten weeks showing complete clearance of lesions with residual post-inflammatory hypopigmentation

Discussion

Angiolymphoid hyperplasia with eosinophilia (ALHE) is an uncommon benign angioproliferative disorder of unknown origin first described by Wells and Whimster in 1969[1]. It is more common in females and presents as a solitary or multiple red-brown papules and nodules.

Although most commonly solitary, multiple lesions can be present in up to 20% of patients [2,3]. The lesions occur predominantly in the head and neck region; extremities are the next most common site. Involvement of other sites like trunk and mucosae is rare. In a review of 116 cases, only 4 cases had truncal involvement [2]. In a recent case series of 7 patients, there were no patients with lesions on the trunk [3]. The growths are often associated with symptoms like pruritus, spontaneous bleeding, and pain. Regional lymphadenopathy is seen in 5-20% of patients and peripheral eosinophilia in 20%. Therefore, neither of these are a pre-requisite for diagnosis [2].

Angiolymphoid hyperplasia with eosinophilia can occur in all races, although it is more frequently reported in Asians, followed by Caucasians. Whether ALHE represents a benign neoplasm or an unusual reactive phenomenon is unclear [2]. Some consider ALHE to be a neoplasm of endothelial cells, but others suggest that the condition is related to an inflammatory vascular reaction

secondary to complex immunologic mechanisms in response to environmental factors such as insect bites, trauma, and infections. Women of child-bearing age are more commonly affected. ALHE can present predominantly as nodules during pregnancy and in patients on oral contraceptive pills [4]. Papules of ALHE have been documented to enlarge and become nodular during pregnancy and decrease in size in the post-partum period, indicating the potential role of hyperestrogenemia as a causative factor [5]. Perimenopause is the period immediately before menopause; it may last a few months to a few years. It is associated with uneven rises and falls in estrogen levels, thus supporting the estrogen theory in this patient. Predominance of T lymphocytes and a re-arrangement of T cell receptors in some cases have made some authors propose that ALHE is a low-grade neoplastic disease secondary to various stimuli [2,6,7]. Histopathological examination has shown damaged and/or tortuous arteries and veins at the base of the lesion, suggesting the role of arteriovenous shunting [2,6].

The major condition in the differential diagnosis of ALHE of the head and neck region is Kimura's disease, which presents as large subcutaneous nodules and plaques with overlying normal skin, associated with regional lymphadenopathy. Serum eosinophil counts and IgE levels are commonly increased [4,8].

Because the lesions occurred on the trunk, the differential diagnoses in our patient included Kaposi's sarcoma, bacillary angiomatosis, and cutaneous lymphoma. The patient had a negative HIV serology and skin biopsy was consistent with ALHE. The proximity to the breast in association with ipsilateral axillary lymphadenopathy also prompted us to investigate for a possible underlying breast malignancy, but all investigations proved negative for this.

The histology of ALHE is quite characteristic. It shows proliferation of large endothelial cells lining vascular spaces with a lymphocytic and eosinophilic inflammatory infiltrate in the dermis. Plump ("epithelioid") endothelial cells show scalloped borders, lobulated nuclei, and vacuolation. These epithelioid cells protrude into the vascular lumen giving a "hobnail" appearance [2,6]. Immunohistochemical study could be useful in some cases. Endothelial cells are positive for Von Willebrand Factor, CD31, and CD34, but negative for keratin. The main lymphocytes are T helper, expressing CD3, CD4, CD43, and CD45RO [7]. Histologically the differential diagnoses of ALHE include epithelioid angiomatous nodule (EAN), epithelioid hemangioendothelioma (EHE), and epithelioid angiosarcoma (EAS). In EAN, the epithelioid cells are polygonal with eosinophilic cytoplasm and enlarged nuclei; they are accompanied by extravasated erythrocytes [9]. Epithelioid hemangioendothelioma is a rare tumor of endothelial cells, which demonstrates proliferation of nests and cords of plump spindle-shaped to epithelioid endothelial cells in a fibromyxoid stroma [10]. Kimura's disease demonstrates prominent lymphoid follicles with germinal centers and fibrosis in the deeper dermis and subcutaneous tissue. Neoangiogenesis with plump endothelial cells are generally absent [6].

The diagnosis of ALHE prior to histology is difficult because of its non-specific morphologic features. In the clinicopathologic study of 116 cases, the clinician offered the diagnosis of ALHE before biopsy in only one instance. The remainder of the pre-biopsy diagnoses covered a spectrum of neoplastic and reactive disorders [2].

The growths have a natural course of either increasing progressively in size or regressing spontaneously. Surgical excision remains the treatment of choice in patients with few lesions [8]. However, recurrences owing to incomplete excision are observed in 30 percent of cases [8]. Other treatment modalities used include electro-dessication, cryotherapy, Moh's micrographic surgery, systemic corticosteroid treatment, intra-lesional injection of corticosteroids or sclerosing agents, photodynamic therapy, interferon alpha-2a, and more recently, pulsed dye laser [11].

Interleukin-5 based treatment is a novel approach. This cytokine interferes with the production and activation of eosinophils, which play a key role in the pathogenesis of ALHE. Imiquimod, which inhibits the production of interleukin 5, and mepolizumab, which inhibits the reaction of IL5 with its receptor, were recently reported to be effective [12,13].

References

1. Wells GC, Whimster IW. Subcutaneous angiolymphoid hyperplasia with eosinophlia. Br J Dermatol 1969;81:1-14.[PMID:5763634]
2. Olsen TG, Helwig EB. Angiolymphoid hyperplasia with eosinophilia. J Am Acad Dermatol 1985;12:781-796.[PMID:4008683]
3. Zaraa I, Milka M, Chouk S et al. Angiolymphoid hyperplasia with eosinophilia: a study of 7 cases. Dermatol online J 2011;17(2):1.[PMID:21382284]
4. Marcum CB, Zager JS, Bélongie IP et al. Profound proliferating angiolymphoid hyperplasia with eosinophilia of pregnancy mimicking angiosarcoma. Cutis 2011;88(3):122-128.[PMID: 22017064]
5. Zarrin-Khameh N, Spoden JE, Tran RM. Angiolymphoid hyperplasia with eosinophilia associated with pregnancy: a case report and review of literature. Arch Pathol Lab Med 2005;129(9):1168-1171.[PMID:16119993]
6. Chun SI, Ji HG. Kimura's disease and angiolymphoid hyperplasia with eosinophilia: clinical and histological differences. J Am Acad Dermatol 1992;27:954-958.[PMID:1479100]

7. Kempf W, Haeffner AC, Zepter K et al. Angiolymphoid hyperplasia with eosinophilia: evidence for a T-cell lymphoproliferative origin. Human Pathology 2002;33:1023-1029.[PMID:12395376]
8. Chong WS, Thomas A, Goh CL. Kimura's disease and angiolymphoid hyperplasia with eosinophilia: two disease entities in the same patient: case report and review of literature. Int J Dermatol 2006;45:139-145.[PMID:16445506]
9. Brenn T, Fletcher CD. Cutaneous epithelioid angiomatous nodule: a disctinct lesion in the morphologic spectrum of epithelioid vascular tumors. Am J Dermatopathol 2004;26(1):14-21.[PMID: 14726818]
10. Clarke LE, Lee R, Militello Get al. Cutaneous epithelioid hemangioendothelioma. J Cutan Pathol 2008;35(2): 236-240.[PMID: 18190452]
11. Vanhooteghem O, Flagothier C, de la Brasinne M. Angiolymphoid hyperplasia with eosinophilia of the scalp: promising results of long-pulsed tunable dye laser treatment. J Eur Acad Dermatol Venereol 2009;23:954-955.[PMID:19453797]
12. Redondo P, Del Olmo J, Idoate M. Angiolymphoid hyperplasia with eosinophilia successfully treated with Imiquimod. Br J Dermatol 2004; 151:1110-1111.[PMID:15541101]
13. Braun-Falco M, Fischer S, Plötz SG et al. Angiolymphoid hyperplasia with eosinophilia treated with anti-interleukin-5 antibody (mepolizumab). Br J Dermatol 2004; 151: 1103-1104.[PMID:15541097]